REMARKS

I Status of the Application

Claims 33-46 and 55-75 are pending in the application.

II. Amended Claim 44 is Definite

Applicants have amended Claim 44 in order to further their business interests and without acquiescing to the Examiner's arguments, and while preserving the right to prosecute the original or similar claims in the future. Applicants respectfully submit that amended Claim 44 is definite. Applicants respectfully request that rejection of Claim 44 under 35 U.S.C § 112 is withdrawn.

III. The Claims are Not Anticipated

The Examiner rejected Claims 33-37, 39-40, 42-44, 46, 55-61 and 63-75 under 35 U.S.C. § 102(b) as alleged being anticipated by Blackburn et al. (U.S. Pat. No. 5,762,948, hereinafter "the '948 patent"). Applicants respectfully disagree.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference."[1] Furthermore, the law requires that the single prior art reference provide an *enabling* disclosure of the claimed invention.[2] Importantly, a prior art reference provides an enabling disclosure only "if the public was in possession of the claimed invention before the date of invention."[3]

The Examiner acknowledges that lysostaphin is not a lantibiotic.[4]

Applicants contend that the '948 patent does not teach a method of decolonizing bacterial populations comprising topically applying to a patient in need thereof at a bacterially infected site a topical composition comprising lysostaphin **and** one or more lantibiotics (e.g., as claimed in Claim 33).

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[1] *Verdegaal Bros. v Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987), and MPEP 2131.
[2] See, e.g., MPEP 2121.01.
[3] See, e.g., MPEP 2121.01.
[4] See Office Action mailed April 10, 2007, page 5.

In stark contrast, **all** of the specific examples of the '948 patent utilize wipes formulated with the lantibiotic nisin (i.e., that do not also contain lysostaphin), and **none** provide any details for decolonizing bacterial populations comprising topically applying to a bacterial infected site a composition comprising lysostaphin and one or more lantibiotics.

Moreover, in addition to failing to provide any support or experimental data for a method of treatment comprising applying a composition comprising both a lantibiotic and lysostaphin, the amount of lantibiotic (nisin) used in the '948 patent (25ug/ml) is actually 0.025% wt% and does not fall into the 0.1 to 10.0 wt% of lantibiotic claimed in the present application.[5] This alone defeats the rejection.

Indeed, the lack of any detail in the '948 patent concerning the use of a composition comprising both a lantibiotic and lysostaphin to decolonize bacterial populations at the site of an infection raises an enablement issue. Applicants respectfully submit that in order to anticipate the presently claimed invention, the prior art reference must provide an *enabling* disclosure of the claimed invention (i.e., it must enable one of ordinary skill in the art to make and use the invention).

However, prior to the disclosure of the present invention, one of ordinary skill in the art would not know whether a composition comprising a lantibiotic and lysostaphin could be used in a method of decolonizing bacterial populations at an infected site.[6] For example, the accompanying Declaration of James J. Mond. M.D., Ph.D. makes clear that in the absence of empirical and/or experimental evidence, one of ordinary skill in the art would not and could not know if the claimed methods of the present invention would work. The Examiner has failed to cite to evidence within the '948 patent, or from any source, that would allow one of ordinary skill in the art background sufficient to practice the instant invention. The '948 patent does not place the public in possession of the claimed invention.

Accordingly, because the '948 patent does not teach or enable a method of applying to a patient a composition comprising a combination of lysostaphin and one or

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[5] See Declaration of James J. Mond, M.D., Ph.D., made under 37 C.F.R. 1.132, submitted herewith, at page 2.

[6] See Declaration of James J. Mond, M.D., Ph.D., made under 37 C.F.R. 1.132, page 2.

more lantibiotics, the '948 patent does not anticipate Claim 33 and claims dependent thereon.

Applicants respectfully request that this rejection be withdrawn.

IV. The Claims are Not Obvious

The Examiner A) maintains the rejection of Claims 33-37, 39-40, 42-44, 46, 55-75 under 35 U.S.C. §103(a) as allegedly being unpatentable over Daley et al. (U.S. Pat. No. 5,342,612, hereinafter "the '612 patent") in view of Blackburn et al. (U.S. Pat. No. 4,980,163, hereinafter "the '163 patent"); B) further rejects Claims 33-40, 42-46, 55-61 and 63-75 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Blackburn et al. (U.S. Pat. No. 5,762,948 (hereinafter "the '948 patent")) in view of Gasson et al. (U.S. Pat. No. 6,448,034 (hereinafter "the '034 patent")); and C) rejects Claim 41 as allegedly being unpatentable over Blackburn et al. (U.S. Pat. No. 5,762,948 (hereinafter "the '948 patent")) and Gasson et al. (U.S. Pat. No. 6,448,034 (hereinafter "the '034 patent")) further in view of Krieger et al. (U.S. Pat. No. 6,503,881 (hereinafter the '881 patent")). Applicants respectfully disagree and contend that the Examiner's allegations are not factually or legally supportable.

In rejecting claims under 35 U.S.C. § 103, the Examiner bears the initial burden of presenting a prima facie case of obviousness.[7] A prima facie case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art.[8] An obviousness analysis requires that the prior art both suggest the claimed subject matter and reveal a reasonable expectation of success to one reasonably skilled in the art.[9]

The test for *prima facie* obviousness is consistent with legal principles enunciated in *KSR Int'l Co. v. Teleflex Inc.,* 127 S. Ct. 1727 (2007). The Federal Circuit summarized the Supreme Court's holding in *KSR* that "While the *KSR* Court rejected a rigid application of the teaching, suggestion, or motivation ("TSM") test, the Court acknowledged the importance of identifying 'a ***reason*** that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new

[7] See In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993).
[8] In re Bell, 991 F.2d 781, 783, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993).
[9] In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

invention does' in an obviousness determination." *Takeda Chem. Indus., Ltd. v. Alphapharma Pty., Ltd., 06-1329, slip op. (Fed. Cir. June 28, 2007)*, at 13-14 (quoting *KSR,* 127 S. Ct. at 1731) (emphasis added). Although the TSM test should not be applied in a rigid manner, it can provide helpful insight to an obviousness inquiry. *KSR,* 127 S. Ct. at 1731. The *KSR* Court upheld the secondary considerations of non-obviounsess, noting that there is "no necessary inconsistency between the idea underlying the TSM test and the *Graham* analysis." *Id.* Additionally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. See M.P.E.P. 2143.

Applicants respectfully submit that the cited references, individually or combined, do not teach or suggest each element of the claimed invention, do not suggest how to modify compositions and methods disclosed therein in order to produce the claimed invention, and do not provide a reasonable expectation of success for carrying out the claimed invention.

A) The '612 and '163 Patents:

Even if Combined[10], The '612 and '163 Patents Do Not Teach All Elements of the Claims, And Do Not Enable One of Ordinary Skill in the Art to Practice the Claimed Invention

Applicants contend that the '612 patent describes compositions comprising lysostaphin in various aqueous surfactant vehicles (e.g., saline, PLURONIC F127, glycerol, poloxamer 407 NF, triacetin, and peanut oil) to potentially produce a lysostaphin with enhanced biological activity and methods of using the composition to enhance lysostaphin bacteriostatic and/or bactericidal efficacy against *S. aureus* .[11]

Applicants further contend that the '612 patent does not provide a teaching or suggestion that a lantibiotic (such as nisin) and lysostaphin be combined in a single formulation.[12] Additionally, the '612 patent actually teaches that addition of various reagents to a composition comprising lysostaphin can inhibit its bactericidal properties.

[10] Applicants believe there exists no proper motivation to combine the references.
[11] See U.S. Pat. No. 5,342,612, Examples 3-5and 9-10.
[12] See Declaration of James J. Mond, M.D., Ph.D., made under 37 C.F.R. 1.132, page 3.

For example, the '612 patent teaches that lysostaphin in an oil base (peanut oil base) loses its bactericidal capacity.[13]

Moreover, the '612 patent does not provide any support (e.g., experimental data) for a method of decolonizing bacteria at a site of an infection comprising topically applying a composition comprising a lantibiotic and lysostaphin.[14] As described in the accompanying Declaration of James J. Mond, M.D., Ph.D., one of ordinary skill in the art would not find examples or experimental data within the '612 patent that would allow one to practice the presently claimed invention.[15] For example, in addition to lacking a teaching or suggestion to generate a composition that comprises both a lantibiotic and lysostaphin, the '612 patent fails to provide any examples of a method of treating bacterial infection with a topical formulation comprising a lantibiotic and lysostaphin. In stark contrast, the '612 patent provides experimental data regarding infusion of lysostaphin (i.e., in the absence of a lantibiotic) into bovine mammary glands.

Accordingly, contrary to the Examiner's allegation, one would not, when looking to the '612 patent for guidance, be motivated to use a composition comprising lystostaphin, nisin, chelating agents and surfactants in a method to decolonize bacterial compositions as presently claimed. The '612 patent does not teach a topical formulation composition comprising a lantibiotic and lysostaphin.

The'163 patent fails to supplement the deficiencies of the '612 patent. In particular, and as described in the accompanying Declaration of James J. Mond, M.D., Ph.D., the '163 patent fails to describe to one of ordinary skill in the art whether a topical formulation comprising a lantibiotic and lysostaphin would or would not be useful in a method of decolonizing bacterial populations at a bacterially infected site.[16] Furthermore, if one of ordinary skill in the art attempted to use the '163 patent as guidance in an effort to carry out the claimed methods of the present invention, the '163 patent would actually teach away from the present invention.[17]

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[13] See Declaration of James J. Mond, M.D., Ph.D., made under 37 C.F.R. 1.132, page 4.
[14] See Declaration of James J. Mond, M.D., Ph.D., made under 37 C.F.R. 1.132, page 3.
[15] See Declaration of James J. Mond, M.D., Ph.D., made unser 37 C.F.R. 1.132, page 4.
[16] See Declaration of James J. Mond, M.D., Ph.D., made unser 37 C.F.R. 1.132, pages 4-5.
[17] See Declaration of James J. Mond, M.D., Ph.D., made unser 37 C.F.R. 1.132, page 5.

Accordingly, neither the '612 patent nor the '163, individually or in combination, teach or enable all of the limitations of the presently claimed invention. Applicants contend that this alone defeats the Examiner's obviousness rejection.

The '612 and '163 Patents Do Not Provide a Reasonable Expectation of Success for Carrying Out the Claimed Invention

The Examiner alleges that "one of skill in the art would reasonably conclude that the compositions of the invention would be effective at decolonizing bacterial populations at bacterially infected sites by topical administration."[18] Applicants contend that this allegation is unfounded and legally unsupportable.

Applicants respectfully submit that no basis has been presented that provides a reasonable expectation of success for a method of decolonizing bacterial populations comprising topically applying to a patient in need thereof at a bacterially infected site a topical composition comprising lysostaphin and one or more lantibiotics (e.g., as recited in Claim 33).

As specifically reviewed above, and as addressed in the accompanying Declaration of James J. Mond, M.D., Ph.D, Applicants respectfully submit that the Examiner has mischaracterized the references. The cited references do not teach or suggest each element of the claimed invention. The cited references individually or collectively further do not enable one of ordinary skill in the art to make and use the claimed invention. Moreover, because the cited references fail to teach one of ordinary skill in the art how to make and use the claimed invention, prior to the disclosure of the present invention, one of skill in the art would have possessed no reasonable expectation of success for carrying out a method of the claimed invention.

Applicants contend that, in effect, the Examiner relies on the '612 and '163 patents to make an "obvious to try" or "obvious to experiment" type rejection.

However, in light of recent Supreme Court and Federal Circuit decisions, a conclusion that the presently claimed invention is prima facie obvious because it is allegedly "obvious to try" is factually and legally unsupportable.

[18] Office Action mailed April 10, page 11.

In *KSR Int'l Co. v. Teleflex Inc.,* 127 S. Ct. 1727 (2007), the Supreme Court specifically noted that, in some circumstances, "the fact that a combination was obvious to try ***might*** show that it was obvious under §103." (emphasis added). The Supreme Court's decision specifically referred to circumstances

> "When there is ***a design need or market pressure to solve a problem*** and there are ***a finite number of identified, predictable solutions***, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. ***In that instance the fact that a combination was obvious to try might show that it was obvious under §103.***" (emphasis added).

Subsequently, and in view of the unanimous Supreme Court decision in KSR, the Federal Circuit reemphasized that

> "[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp." KSR, 127 S. Ct. at 1732. In such circumstances, 'the fact that a combination was obvious to try might show that it was obvious under § 103.' Id."[19]

However, the Federal Circuit, following the guidance of the Supreme Court, distinguished the circumstances of KSR from those before it in Takeda Chemical.

In Takeda Chemical, the appellant, Alphapharma, argued in a Declaratory Judgment action that a claimed chemical compound was an obvious modification of a previously known compound, the modification requiring the substitution of a homolog in a different ring position.[20] Specifically, and in an attempt to seize upon the Supreme Court's acknowledgment that a combination of elements that are obvious to try might support obviousness under § 103, Alphapharma argued to the Federal Circuit that the claimed compounds would have been obvious because the prior art compound fell within "the object reach of the claim," and the evidence demonstrated that using the techniques of homologation and ring-walking would have been "obvious to try."

The Federal Circuit rejected Alphapharm's arguments and held that in view of KSR, in circumstances in which the prior art disclosed a broad selection of compounds any one of which could have been selected as a lead compound for further investigation,

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[19] See *Takeda Chemical Industries v. Alphapharm, No. 06-1329, slip op. (Fed. Cir. June 28, 2007)*, at 15.
[20] Id.

the prior art does not provide a predictable solution…Thus, this case fails to present the type of situation contemplated by the [Supreme] Court when it stated that an invention may be deemed obvious if it was "obvious to try." The evidence showed that it was not obvious to try."[21]

In the case at hand, Applicants have presented the teachings present in the disclosures of the '612 and '163 patents.[22] In particular, the disclosures provide a broad array of various compounds any one of which could be combined with another by one of ordinary skill in the art for use in a topical formulation for further investigation. For example, one could select as reagents to be combined in a topical formulation any one of a broad and diverse type of enzyme or bacteriostatic peptide, antibiotic, chelating agent, and/or surfactant.

Thus, an argument that the cited references render the claimed invention prima facie obvious because it might appear obvious to try (e.g., obvious to try to select any one of a number of compounds from a broad selection of compounds in a combination for use in a topical formulation for use in a method of decolonizing bacterial populations at the site of an infection) is not legally supportable. The cited references do not provide a predicable solution for treating a patient among the millions of possible combinations.[23] The Federal Circuit has expressly identified that this type of argument falls outside the scope of the situation contemplated by the Supreme Court in KSR when the Court stated that an invention may be deemed obvious if it was "obvious to try."

B and C) The '948, '034 and '881 Patents

Applicants have described the '948 patent above. Additionally, James J. Mond, M.D., Ph.D., describes the teachings of the '948 patent in the Declaration submitted herewith. The '948 patent fails to teach, suggest or enable all elements of the presently claimed invention. In particular, the '948 patent "does not provide any support or

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[21] Id.

[22] See, e.g., Response to Office Action filed December 21, 2006, page 17, lines 1-9, discussing the fact that the '612 patent provides a laundry list of antimicrobial agents that may also benefit from combination with an aqueous surfactant vehicle including a bacteriolytic peptide such as an enzyme or bacteriostatic peptide, for example, lysostaphin, lysozyme, nisin, magainins …or may be formulated with antibiotics such as amoxicillin, ampicillin, cephapirin, cloxacillin, hetacillin, penicillin G, etc. (U.S. Pat. No. 5,342,612, columns 3 and 4, lines 30-40 and 4-15, respectively).

[23] See Declaration of James J. Mond, M.D., Ph.D., made unser 37 C.F.R. 1.132, pages 2-4.

experimental data using a composition that has both lysostaphin and a lantibiotic. Also, the amount of lantibiotic (nisin) used by Blackburn (25ug/ml) is actually 0.025% wt% and does not fall into the 0.1 to 10.0 wt% of lantibiotic that is claimed in the present application. Furthermore, Blackburn only provides examples for using wipes formulated with nisin and does not provide any examples or experimental evidence using liquid formulations (separate from a wipe) as alleged by the examiner."[24]

The '034 and '881 patents do not supplement the deficiencies of the '948 patent. Neither the '034 patent or the '881 patent mention or even reference lysostaphin. Moreover, one of ordinary skill in the art would not consult either of these references in an attempt to generate the methods of the present invention.[25]

Accordingly, the cited references do not render the present invention obvious. Applicants request that the rejections are withdrawn and the claims are passed to allowance.

V. Rejection of the Specification Under MPEP 608.

Applicants have herein amended the Specification in order to comply with MPEP 608 and 37 C.F.R. 1.57. In particular, Applicants have amended the Specification to insert reference to U.S. Pat. App. Pub. No. 20050118159 published on June 2, 2005.

This correction inserts material by amendment previously incorporated by reference as WO 03/82124. No new matter has been added (37 C.F.R. 1.57(f)).

VI. New Rejection Under 35 U.S.C. § 112

Claim 34

The Examiner rejected Claim 34. Applicants respectfully disagree. Nonetheless, Applicants have amended Claim 34 in order to further the prosecution of the present application without acquiescing to the Examiner's arguments and while preserving the right to prosecute the original, or similar, claim in the future. Applicants respectfully

[24] See Declaration of James J. Mond, M.D., Ph.D., made unser 37 C.F.R. 1.132, page 5.
[25] See Declaration of James J. Mond, M.D., Ph.D., made unser 37 C.F.R. 1.132, page 5.

submit that amendment to Claim 34 renders the Examiner's rejection moot. Applicants respectfully request the Examiner withdraw the rejection of Claim 34.

Claim 41.

The Examiner rejected Claim 41. Applicants respectfully disagree. Nonetheless, Applicants have amended Claim 41 in order to further the prosecution of the present application without acquiescing to the Examiner's arguments and while preserving the right to prosecute the original, or similar, claim in the future. Applicants respectfully submit that amendment to Claim 41 renders the Examiner's rejection moot. Applicants respectfully request the Examiner withdraw the rejection of Claim 41.

Claim 45.

The Examiner rejected Claim 45. Applicants respectfully disagree. Nonetheless, Applicants have amended Claim 45 in order to further the prosecution of the present application without acquiescing to the Examiner's arguments and while preserving the right to prosecute the original, or similar, claim in the future. Applicants respectfully submit that amendment to Claim 45 renders the Examiner's rejection moot. Applicants respectfully request the Examiner withdraw the rejection of Claim 45.

Claim 63.

The Examiner rejected Claim 63. Applicants respectfully disagree. Nonetheless, Applicants have amended Claim 63in order to further the prosecution of the present application without acquiescing to the Examiner's arguments and while preserving the right to prosecute the original, or similar, claim in the future. Applicants respectfully submit that amendment to Claim 63 renders the Examiner's rejection moot. Applicants respectfully request the Examiner withdraw the rejection of Claim 63.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that Applicants have addressed all grounds for rejection and Applicants' claims should be passed to allowance.

Reconsideration of the application is respectfully requested. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourages the Examiner to call the undersigned collect at (608) 218-6900.

Respectfully submitted,

Date: October 10, 2007

/Tyler J. Sisk/
Tyler J. Sisk
Registration No. 59,850

CASIMIR JONES, S.C.
440 Science Drive, Suite 203
Madison, Wisconsin 53711
608/218-6900